123 is indicated by brackets and matter that has been added is indicated by underlining. A clean version of the pending claims, as amended, is attached hereto as Exhibit B.

Please amend the claims as follows:

Please amend claims 1, 18, 26, 29, 38, 50, 64, 96, 106 and 123 to read as follows:

1. (Five Times Amended) A method of determining a consensus profile for a first plurality of drug perturbations to a cell type or organism, said method comprising determining, for each of a plurality of sets of cellular constituents in a plurality of response profiles, said set of cellular constituents is upregulated or downregulated by said first plurality of drug perturbations, each response profile in said plurality of response profiles (i) comprising measurements of a plurality of cellular constituents, and (ii) resulting from a different drug perturbation among said first plurality of drug perturbations to said type of cell or organism, wherein each set of cellular constituents in said plurality of sets of cellular constituents consists of cellular constituents that co-vary under a second plurality of perturbations or that are co-regulated, wherein said plurality of response profiles comprises at least five response profiles, and wherein said consensus profile for said first plurality of drug perturbations comprises measurements of said set or sets of cellular constituents that are determined in said determining step to be upregulated or downregulated by said first plurality of drug perturbations.

18. (Twice Amended) The method of claim 17, wherein said cluster analysis is carried out by a hierarchical clustering method, and wherein the objective statistical test comprises:

(a) determining for each cluster generated by said cluster analysis an actual fractional improvement in the cluster analysis of the cellular constituents based on the unpermuted responses of said cellular constituents, wherein said fractional improvement is an improvement in total scatter with respect to a cluster center in going from one cluster to two clusters;

(b) generating permuted responses of cellular constituents by means of Monte Carlo randomization of perturbation index for the response of each cellular constituent across all perturbations;

(c) performing said cluster analysis on the permuted responses of cellular constituents;

(d) determining for each cluster generated in step (c) the fractional improvement in the cluster analysis of cellular constituents based on the permuted responses of cellular constituents, wherein said fractional improvement is an improvement in total scatter with respect to a cluster center in going from one cluster to two clusters: and

(e) repeating steps (b) through (d) so that a distribution of fractional improvements in the cluster analysis of the cellular constituents is obtained for each said cluster generated by said cluster analysis;

wherein the statistical significance of each of said sets of co-varying cellular constituents is determined by comparing the actual fractional improvement for the corresponding cluster to the distribution of fractional improvements for the corresponding cluster.

26. (Twice Amended) The method of claim 25, wherein said cluster analysis is carried out by a hierarchical clustering method, and wherein the objective statistical test comprises:

(a) determining for each cluster generated by said cluster analysis an actual fractional improvement in the cluster analysis of the unpermuted response profiles, wherein said fractional improvement is an improvement in total scatter with respect to a cluster center in going from one cluster to two clusters;

(b) generating permuted response profiles by means of Monte Carlo randomization of cellular constituent index for each response profile across the measured cellular constituents;

(c) performing said cluster analysis on the permuted response profiles;

(d) determining for each cluster generated in step (c) the fractional improvement in the cluster analysis of the permuted response profiles, wherein said fractional improvement is an improvement in total scatter with respect to a cluster center in going from one cluster to two clusters; and

(e) repeating steps (b) through (d) so that a distribution of fractional improvements in the cluster analysis of the response profiles is obtained for each said cluster generated by said cluster analysis;

wherein the statistical significance of each of said sets of response profiles is determined by comparing the actual fractional improvement for the corresponding cluster to the distribution of fractional improvements for the corresponding cluster.

29. (Three Time Amended) A method of determining a consensus profile for a first plurality of perturbations to a cell type or organism, said method comprising determining, for each of a plurality of sets of cellular constituents in a plurality of projected profiles, whether said set of cellular constituents is upregulated or downregulated by said first plurality of perturbations, each projected profile in said plurality of projected profiles

(i) resulting from a different perturbation among said first plurality of perturbations to said type of cell or organism, and

(ii) comprising measurements of a plurality of cellular constituents in said type of cell or organism that have been projected onto basis cellular constituent sets, said basis cellular constituent sets being defined by co-variation of measurements of cellular constituents under a second plurality of different perturbations, wherein said consensus profile for said first plurality of perturbations comprises projected measurements of said set or sets of cellular constituents that are determined in said determining step to be upregulated or downregulated by said first plurality of perturbations.

38. (Four Times Amended) A method of determining a consensus profile for a first plurality of perturbations to a cell type or organism, said method comprising determining, for each of a plurality of sets of genes in a plurality of response profiles,whether said set of genes upregulated or downregulated by said first plurality of perturbations, each response profile in said plurality of response profiles (i) comprising measurements of transcript levels for a plurality of genes, and (ii) resulting from a different perturbation among said first plurality of perturbations to said type of cell or organism, wherein each set of genes in said plurality of sets of genes consists of genes having transcripts that co-vary under a second plurality of perturbations or that are co-regulated, and wherein said consensus profile for said first plurality of perturbations comprises measurements of transcript levels for said set or sets of genes that are determined in said determining step to be upregulated or downregulated by said first plurality of perturbations.

50. (Twice Amended) The method of claim 49, wherein said cluster analysis is carried out by a hierarchical clustering method, and wherein the objective statistical test comprises:

(a) determining for each cluster generated by said cluster analysis an actual fractional improvement in the cluster analysis of the unpermuted response profiles, wherein said fractional improvement is an improvement in total scatter with respect to a cluster center in going from one cluster to two clusters;

(b) generating permuted response profiles by means of Monte Carlo randomization of gene index for each response profile across the measured genes;

(c) performing said cluster analysis on the permuted response profiles;

(d) determining for each cluster generated in step (c) the fractional improvement in the cluster analysis of the permuted response profiles, wherein said fractional improvement is an improvement in total scatter with respect to a cluster center in going from one cluster to two clusters; and

(e) repeating steps (b) through (d) so that a distribution of fractional improvements in the cluster analysis of the response profiles is obtained for each cluster generated by said cluster analysis;

wherein the statistical significance of each of said sets of response profiles is determined by comparing the actual fractional improvement for the corresponding cluster to the distribution of fractional improvements for the corresponding cluster.

64. (Twice Amended) The method of claim 63, wherein said cluster analysis is carried out by a hierarchical clustering method, and wherein the objective statistical test comprises:

(a) determining for each cluster generated by said cluster analysis an actual fractional improvement in the cluster analysis of cellular constituents based on the unpermuted responses of said cellular constituents, wherein said fractional improvement is an improvement in total scatter with respect to a cluster center in going from one cluster to two clusters;

(b) generating permuted responses of cellular constituents by means of Monte Carlo randomization of the perturbation index for each cellular constituent across all perturbations;

(c) performing said cluster analysis on the permuted responses of cellular constituents;

(d) determining for each cluster generated in step (c) the fractional improvement in the cluster analysis of cellular constituents based on the permuted responses of cellular constituents, wherein said fractional improvement is an improvement in total scatter with respect to a cluster center in going from one cluster to two clusters; and

(e) repeating steps (b) through (d) so that a distribution of fractional improvements in the cluster analysis of the cellular constituents is obtained for each cluster generated by said cluster analysis;

wherein the statistical significance of each of said sets of cellular constituents is determined by comparing the actual fractional improvement for the corresponding cluster to the distribution of fractional improvements for the corresponding cluster.

72. (Three Times Amended) A method for analyzing response data from a biological sample comprising

(a) grouping cellular constituents from the biological sample into sets of genes that co-vary in a plurality of response profiles, each response profile in said plurality of response profiles (i) comprising measurements of transcript levels of a plurality of genes, and (ii) resulting from a different perturbation to said biological sample; and

(b) grouping the plurality of response profiles into sets of response profiles that similarly affect genes,

wherein said plurality of response profiles comprises at least five response profiles.

73. (Amended) The method of claim 72, wherein one or more genes which co-vary in association with a particular biological effect are identified from the sets of genes that co-vary in said plurality of response profiles.

74. (Amended) The method of claim 72, wherein one or more response profiles that are associated with a particular biological effect are identified from the sets of response profiles that similarly affect genes.

75. The method of claim 73 or 74, wherein the particular biological effect is an effect on a biological pathway.

76. (Amended) The method of claim 73, wherein one or more genes associated with said biological effect are identified.

77. The method of claim 76 wherein the one or more genes identified comprise known genes.

78. The method of claim 76, wherein the one or more genes identified comprise previously unknown genes.

89. The method of claim 1, wherein said sets of cellular constituents are co-varying cellular constituent sets.

90. The method of claim 89, wherein the cellular constituents which co-vary are identified by cluster analysis.

91. The method of claim 89, wherein the cluster analysis is done by means of a clustering algorithm.

92. The method of claim 91, wherein the clustering algorithm is *hclust*.

93. The method of claim 90, wherein said cluster analysis determines a clustering tree, the cellular constituents which co-vary comprising branches of said clustering tree.

94. The method of claim 93, wherein the sets of co-varying cellular constituents are selected from a branching level of the clustering tree.

95. The method of claim 90, wherein a statistical significance for the sets of co-varying cellular constituents is determined by means of an objective statistical test.

96. (Amended) The method of claim 95, wherein said cluster analysis is carried out by a hierarchical clustering method, and wherein the objective statistical test comprises:

(a) determining for each cluster generated by said cluster analysis an actual fractional improvement in the cluster analysis of the cellular constituents based on the unpermuted responses of said cellular constituents, wherein said fractional improvement is an improvement in total scatter with respect to a cluster center in going from one cluster to two clusters;

(b) generating permuted responses of cellular constituents by means of Monte Carlo randomization of the perturbation index for response of each cellular constituent across the set of perturbations;

(c) performing said cluster analysis on the permuted responses of cellular constituents;

(d) determining for each cluster generated in step (c) the fractional improvement in the cluster analysis of cellular constituents based on the permuted response responses of cellular constituents, wherein said fractional improvement is an improvement in total scatter with respect to a cluster center in going from one cluster to two clusters; and

(e) repeating steps (b) through (d) so that a distribution of fractional improvements in the cluster analysis of the cellular constituents is obtained for each cluster generated by said cluster analysis,

wherein the statistical significance of each of said sets of co-varying cellular constituents is determined by comparing the actual fractional improvement for the corresponding cluster to the distribution of fractional improvements for the corresponding cluster.

106. (Amended) The method of claim 105, wherein said cluster analysis is carried out by a hierarchical clustering method, and wherein the objective statistical test comprises:

(a) determining for each cluster generated by said cluster analysis an actual fractional improvement in the cluster analysis of the unpermuted response profiles, wherein said fractional improvement is an improvement in total scatter with respect to a cluster center in going from one cluster to two clusters;

(b) generating permuted response profiles by means of Monte Carlo randomization of cellular constituent index for each response profile across the measured cellular constituents;

(c) performing said cluster analysis on the permuted response profiles;

(d) determining for each cluster generated in step (c) the fractional improvement in the cluster analysis of the permuted response profiles, wherein said fractional improvement is an improvement in total scatter with respect to a cluster center in going from one cluster to two clusters; and

(e) repeating steps (b) through (d) so that a distribution of fractional improvements in the cluster analysis of the response profiles is obtained for each cluster generated by said cluster analysis;

wherein the statistical significance of each of said sets of response profiles is determined by comparing the actual fractional improvement for the corresponding cluster to the distribution of fractional improvements for the corresponding cluster.

123. (Amended) The method of claim 122, wherein said cluster analysis is carried out by a hierarchical clustering method, and wherein the objective statistical test comprises:

(a) determining for each cluster generated by said cluster analysis an actual fractional improvement in the cluster analysis of the genes based on the unpermuted responses of said genes, wherein said fractional improvement is an improvement in total scatter with respect to a cluster center in going from one cluster to two clusters;